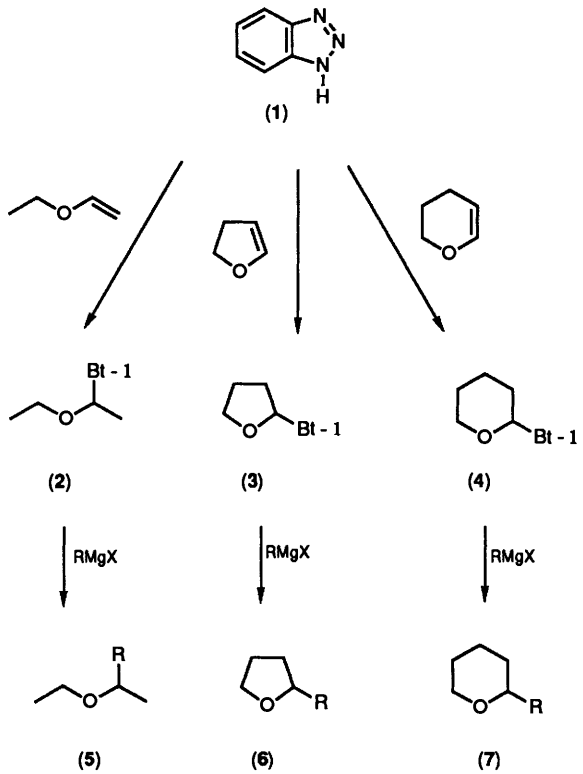
Addition of Benzotriazole to Vinyl Ethers. Chemistry of the Adducts

Alan R. Katritzky,* Stanislaw Rachwal, and Bogumila Rachwal
Department of Chemistry, University of Florida, Gainesville, Florida 32611 USA

Benzotriazole adds readily to ethyl vinyl ether, to 2,3-dihydrofuran, and to 3,4-dihydro-2*H*-pyran to form the respective α-benzotriazolyl ethers. Reactions of benzotriazole with α-methoxy derivatives of tetrahydrofuran and tetrahydropyran give similar products by substitution of benzotriazolyl for the methoxy groups. The corresponding adducts of benzotriazole and vinyl acetates are unstable and eliminate acetate anion to form geminal bis(benzotriazolyl)alkanes. The products show benzotriazol-1-yl to -2-yl isomerization. α-Benzotriazolyl derivatives of tetrahydrofuran and tetrahydropyran react with phenyl- and alkynyl-magnesium reagents to give the respective α-phenyl or α-alkynyl cycloethers. Alkylmagnesium halides by contrast attack the benzotriazolyl N-3 atom of these adducts and open the tetrahydropyranyl ring with formation of an *N,N'*-disubstituted *o*-phenylenediamine. ^{1}H and ^{13}C NMR spectra of the products are discussed.

We recently disclosed general, versatile, and high-yielding methods for the preparation of a wide variety of dialkyl and aryl alkyl ethers from 1-(α-alkoxyalkyl)benzotriazoles.[1] The latter were obtained by several alternatives routes: (i) from benzotriazole, an aldehyde, and an alcohol, with water removal; (ii) from a 1-(α-chloroalkyl)benzotriazole and an alkoxide; (iii) from an acetal or ketal with benzotriazole. We have now found that benzotriazole adds readily to vinyl ethers to give a further route to 1-(α-alkoxyalkyl)benzotriazoles, thus providing a synthetic transformation of unsaturated ethers into their saturated analogues, which is of special utility for cyclic derivatives.

Reactions of vinyl ethers with nucleophiles under acidic catalysis are well known. Thus, 3,4-dihydro-2*H*-pyran with alcohols in the presence of an acid readily forms the corresponding 2-alkoxytetrahydropyrans in high yields. This is widely utilized to protect hydroxy groups in polyfunctional molecules, especially in the synthesis of natural products, *e.g.* antibiotics,[2-5] insect sex pheromones,[6,7] steroids,[8-10] and pharmacological agents.[11-13] 2,3-Dihydrofuran[14-17] and ethyl vinyl ether[17] give similar adducts. Instead of an acid, iodotrimethylsilane can be used as a catalyst for addition of alcohols to 3,4-dihydro-2*H*-pyran, providing mild, neutral conditions for the reaction.[18] Additions of azoles, *e.g.* 2-nitroimidazole,[19] purines,[20] and indazoles,[21] and of uracils[22-25] to 2,3-dihydrofuran or to 3,4-dihydro-2*H*-pyran with formation of *N*-(2-tetrahydrofuranyl) or *N*-(2-tetrahydropyranyl) groups, respectively, also requires acidic catalysis, whereas phenylsulphinic acid[26,27] adds to 3,4-dihydro-2*H*-pyran spontaneously without any catalyst.

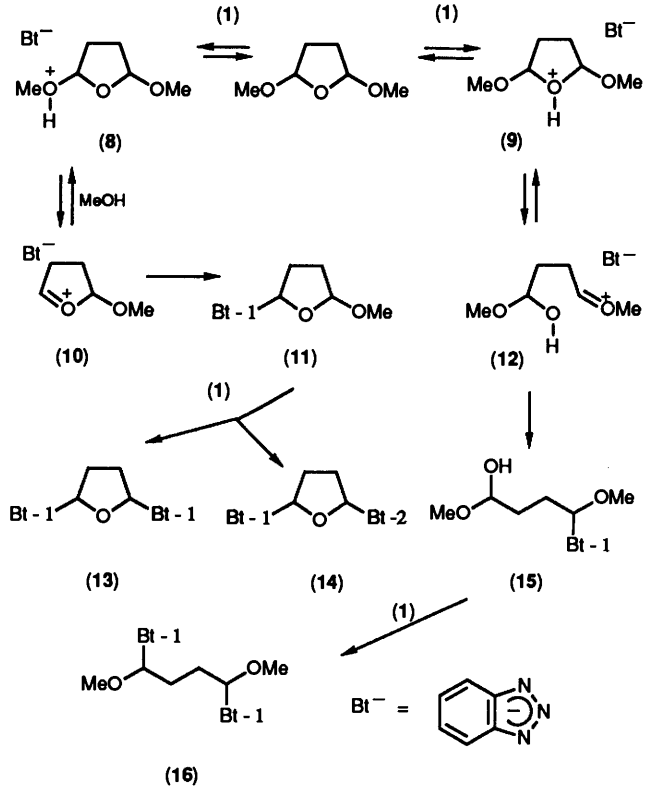


Scheme 1. Bt-1 = benzotriazol-1-yl and Bt-2 = benzotriazol-2-yl.

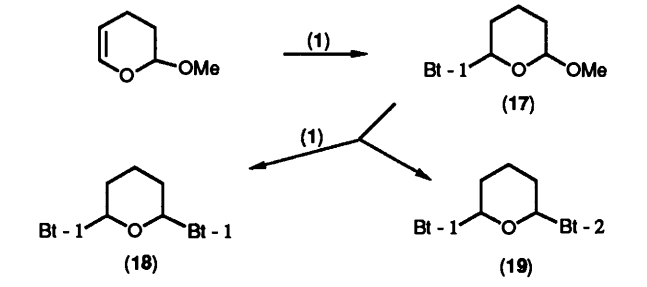
Results and Discussion

Reactions of Vinyl Ethers and Esters with Benzotriazole.— Benzotriazole (**1**) adds readily to ethyl vinyl ether, to 2,3-dihydrofuran, and to 3,4-dihydro-2*H*-pyran at 25 °C to form the respective α-benzotriazolyl ethers, (**2**), (**3**), and (**4**) (Scheme 1). Preparative scale reactions were conveniently carried out in refluxing carbon tetrachloride, reducing the reaction time to 2 h and allowing NMR monitoring of samples of the reaction mixture.

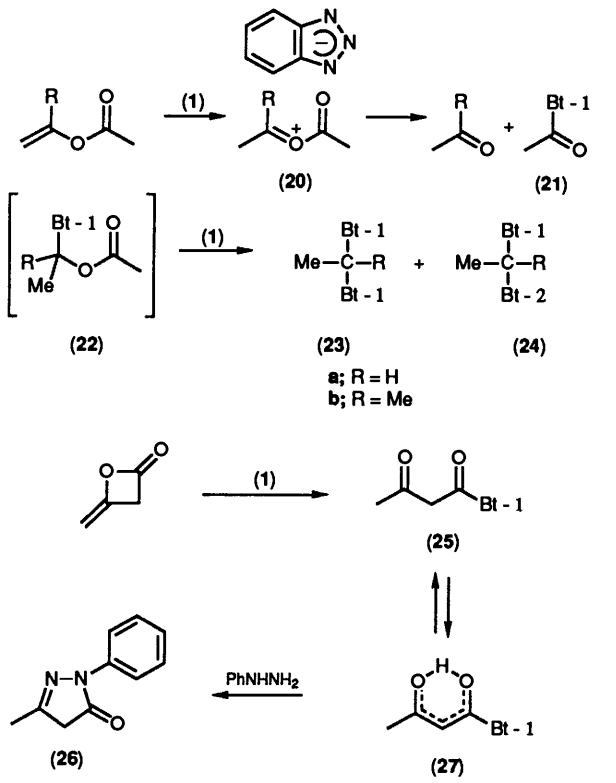
Substitution of an α-methoxy group in the tetrahydrofuranyl system by benzotriazolyl leads to similar adducts. Adduct (**11**) from 2,5-dimethoxytetrahydrofuran can further react with a second molecule of benzotriazole yielding an isomeric mixture of 2,5-bis(benzotriazol-1-yl)tetrahydrofuran (**13**) and 2-(benzotriazol-1-yl)-5-(benzotriazol-2-yl)tetrahydrofuran (**14**) (Scheme 2). 1,4-Bis(benzotriazol-1-yl)-1,4-dimethoxybutane (**16**) is found in the reaction mixture as an additional product. Thus, the reaction can take two alternative courses. In the first, 2,5-dimethoxytetrahydrofuran is protonated at the methoxy group by benzotriazole (pK_a 8.2),[28] then eliminates methanol to yield cation (**10**), which adds the benzotriazolyl anion to form (**11**). This sequence when repeated with the second methoxy group leads finally to isomeric bis-adducts (**13**) and (**14**). Alternatively, protonation of the ring oxygen atom leads to an open form (**12**), which after addition of the benzotriazolyl anion and reaction of the hemiacetal (**15**) with another molecule of benzotriazole, finally gives (**16**). Surprisingly, no opening of the tetrahydro-



Scheme 2. Bt-1 = benzotriazol-1-yl and Bt-2 = benzotriazol-2-yl.



Scheme 3. Bt-1 = benzotriazol-1-yl and Bt-2 = benzotriazol-2-yl.



Scheme 4. Bt-1 = benzotriazol-1-yl and Bt-2 = benzotriazol-2-yl.

furan ring was reported in the reaction of 2,5-dimethoxytetrahydrofuran with benzenesulphinic acid.[29]

Addition of benzotriazole to 2-methoxy-3,4-dihydro-2*H*-pyran leads to stable 2-methoxy-6-(benzotriazol-1-yl)tetrahydropyran (**17**) (Scheme 3). Prolonged heating of adduct (**17**) with benzotriazole in the presence of a catalytic amount of a strong acid caused substitution of the methoxy group by the benzotriazolyl substituent, with formation of a mixture of isomers (**18**) and (**19**) in a ratio of 5:1. Taking advantage of the higher polarity of benzotriazol-1-yl derivatives compared with the -2-yl analogues, adducts (**18**) and (**19**) were separated by column chromatography.

Vinyl acetates also react with benzotriazole, but instead of the expected adducts (**22**) (Scheme 4), mixtures of 1-acetylbenzotriazole (**21**) and bis-adducts (**23**) and (**24**), were formed. All these reactions start with protonation at the β-carbon atom to give cations of type (**20**). Nucleophilic attack of the benzotriazolyl anion on the carbonyl group of (**20**) leads to formation of 1-acetylbenzotriazole (**21**), and acetaldehyde (R = H) or acetone (R = Me). The main reaction, however, is an attack of the benzotriazolyl anion on the α-carbon of (**20**) giving (**22**), which [unlike (**5**)], spontaneously loses acetate anion to yield the corresponding benzotriazolyl carbonium ion. This adds more benzotriazole to form the geminal bis(benzotriazolyl)alkanes (**23**) or (**24**). The driving force of this reaction is the higher stability of the acetate anion in comparison to the ethoxy anion which would have to be released from (**5**).

Diketene, which can be treated as a vinyl ester, reacts spontaneously with benzotriazole giving a solid material, which, by NMR spectroscopy, was recognized as a mixture of ketone (**25**) (characteristic singlets at δ 2.43 and 4.56, methyl and methylene groups, respectively) and its tautomeric enol form (**27**) (characteristic singlets at δ 2.19 and 6.64, methyl and vinyl protons, respectively) in a ratio of 3:4. A reaction mechanism analogous to that which produces acetylbenzotriazole (**21**) from vinyl acetates must be involved here. The adduct (**25**) is sufficiently stable for analysis, but hydrolyses in air to benzotriazole. Support for structures (**25**) and (**26**) was obtained by reaction with phenylhydrazine giving the known pyrazolone (**26**).[30,31]

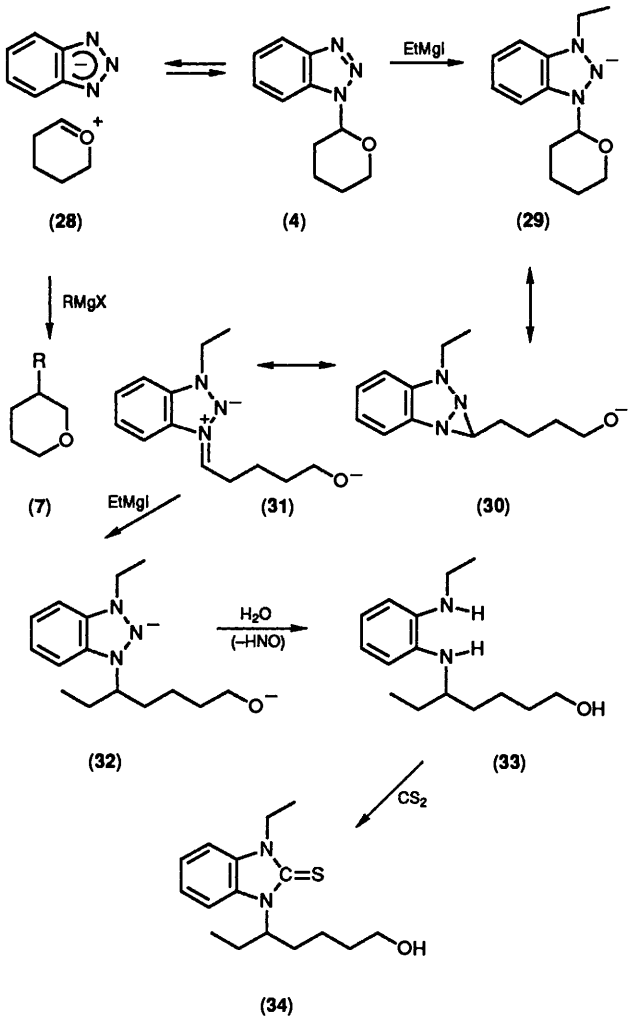
Reactions of the Adducts with Grignard Reagents.—The α-benzotriazolyl ethers [(**2**), (**3**), and (**4**)] were treated with Grignard reagents under the conditions previously described[1] giving ethers of types (**5**), (**6**), and (**7**), respectively (Scheme 1). The yields of cyclic ethers (**6**) and (**7**) (Table 1) were lower, however, than those we obtained for acyclic analogues applying a similar procedure,[1] probably because side products were formed by ring opening of (**3**) and (**4**).

2-Benzotriazolyltetrahydropyran (**4**) is especially sensitive to alkyl Grignard reagents: reaction with ethylmagnesium iodide at 20 °C in ether gave only ring-opened product (**33**) (Scheme 5). Formation of (**33**) can be explained by double Grignard attack on C_α and N-3 in molecules of (**4**), similar to the mechanism described before for simple (benzotriazol-1-yl)-methyl ethers.[1] Regular Grignard reaction of α-benzotriazol-1-yl) ethers requires initial ionization of the benzotriazolyl C–O bond; compound (**4**) thus forms cation (**28**) which then reacts

Table 1. Products obtained from ethyl vinyl ether, dihydrofuran, and dihydropyran (2)–(7).

Compd.	R	Molecular formula	Yield (%)	M.p. (°C) or b.p. (°C/mmHg)	Found (calcd.) (%) C	H	N	HR MS ($M^+ - H$) Found (calcd.)
(2)	Bt	$C_{10}H_{13}N_3O$	100	Oil				191.1051 (191.1058)
(3)	Bt	$C_{10}H_{11}N_3O$	100	Oil				189.0906 (189.0902)
(4)	Bt	$C_{11}H_{13}N_3O$	100	54–55	65.05 (65.00)	6.45 (6.44)	20.75 (20.67)	
(5)	Hexyl	$C_{10}H_{22}O$	65	Oil				157.1591 (157.1592)
(6a)	Hexyl	$C_{10}H_{20}O$	59[a]	Oil		Ref. 34		
(6b)	Ph	$C_{10}H_{12}O$	66	Oil		Ref. 29		
(6c)	PhC≡C	$C_{12}H_{12}O$	78	Oil		Ref. 29		
(6d)	BuC≡C	$C_{10}H_{16}O$	90[a]	67–68/0.35	78.65 (78.90)	10.7 (10.59)	— —	
(7a)	Ph	$C_{11}H_{14}O$	55	Oil		Ref. 29		
(7b)	PhC≡C	$C_{13}H_{14}O$	84	Oil		Ref. 29		
(7c)	BuC≡C	$C_{11}H_{18}O$	78[a]	54–55/0.08		Ref. 34		

[a] Yield based on ^1H NMR spectrum. Other values are isolated yields.



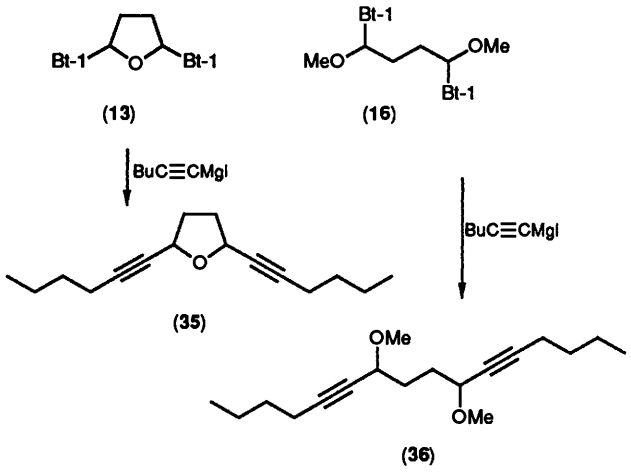
Scheme 5.

with the Grignard reagent giving (7). However, at the elevated temperatures required to obtain substantial quantities of ion (28), strongly nucleophilic alkyl Grignard reagents also attack the benzotriazolyl N-3 atom giving anion (29) which can exist in the solution in a relatively high concentration, being stabilized by a cyclic form (30) and ylide (31). Ylide (31) is attacked by a second Grignard reagent giving adduct (32) which is hydrolysed, during the work-up, to the *o*-phenylenediamine derivative (33). For a proof of structure, (33) was transformed, by condensation with carbon disulphide, into the benzimidazole-2-thione (34).

Phenylmagnesium bromide behaved as a less aggressive reagent giving 2-phenyltetrahydrofuran (6b) and 2-phenyltetrahydropyran (7a) in relatively good yields (Table 1). Quite high yields of 2-alkynyltetrahydro-furans and -pyrans were obtained from reactions of (3) and (4), respectively, with iodomagnesium acetylenides (Table 1). These observations indicate that the nature of the Grignard reagent, and especially its nucleophilicity, has a dramatic influence on its mode of reaction with 2-(benzotriazol-1-yl) derivatives of tetrahydrofuran and tetrahydropyran.

Reactions similar to these substitutions of the benzotriazolyl group at the α-positions of tetrahydrofuran and tetrahydropyran have been reported in the literature. Thus, Grignard reactions of 2-chlorotetrahydropyrans,[32] or 2-aryloxytetrahydropyrans[33] with alkyl Grignard reagents give the corresponding 2-alkyltetrahydropyrans in high yields. Reactions of 2-phenylsulphonyltetrahydrofuran and 2-phenylsulphonyltetrahydropyran with a phenylzinc reagent[29] form 2-phenyltetrahydrofuran (6b) and 2-phenyltetrahydropyran (7a) in 78 and 90% yields, respectively. The same sulphones are converted by an organozinc reagent from phenylacetylene into 2-phenylethynyl-tetrahydrofuran (6c) and -tetrahydropyran (7b) in 88 and 97% yield,[29] respectively. 2-Chlorotetrahydropyran reacted with the hex-1-ynylmagnesium reagent to give 2-(hex-1-ynyl)tetrahydropyran (7c) with 50% yield.[34] 2-Alkyl- and 2-aryl-tetrahydro-furans and -pyrans are generally prepared by cyclization of the appropriate diols, *e.g.*, 4-hydroxydecan-1-ol gives 2-hexyltetrahydrofuran (6a) in 70% yield.[34] The results of Table 1 are competitive with the best literature methods described above because of the simple procedure and the stability of the benzotriazolyl adducts (in comparison, *e.g.*, with α-chloro ethers).

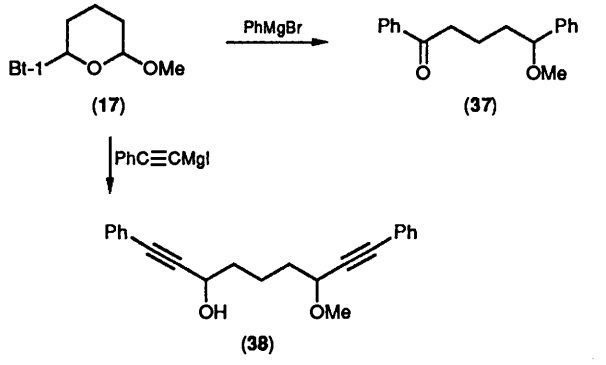
Reactions of the 2,5-disubstituted tetrahydrofuran (13) and (14) with alkyl Grignard reagents gave complex mixtures of acyclic products. However, hex-1-ynylmagnesium iodide substituted the benzotriazolyl groups in (13) and (14) to give



Scheme 6.

(35) smoothly, without opening the sensitive ether ring (Scheme 6). 1,4-Bis(benzotriazol-1-yl)-1,4-dimethoxybutane (16) present in the mixture with (13) and (14), was transformed into hexadecadiyne (36) in this reaction.

Treatment of the tetrahydropyran derivative (17) with organomagnesium reagents gave exclusively ring-opened products. A nucleophilic cleavage mechanism, similar to that discussed for the cleavage of cycloethers with soft organolithium compounds,[54] is probably involved. Thus, 5-methoxy-1,5-diphenylpentan-1-one (37) (Scheme 7) was separated by column



Scheme 7.

chromatography from a reaction of (17) with phenylmagnesium bromide. The oxidation level of C-1 in (37) indicates that the molecule could not be formed by a simple Grignard substitution/ring-opening procedure. Initially formed 5-methoxy-1,5-diphenylpentan-1-ol is probably oxidized to the ketone (37); alkyl phenyl carbinols show considerable reducing ability.[55] No such oxidation was observed in the reaction of (17) with phenylethynylmagnesium iodide which leads to 7-methoxy-1,9-diphenylnona-1,8-diyn-3-ol (38).

Spectral Characterization of the obtained Compounds: The Problem of Isomerization.—^{1}H and ^{13}C NMR spectra of mono- and di-substituted tetrahydro-furans and -pyrans have been extensively analysed as models for the chemistry of saccharides.[35,36] ^{1}H NMR data for the benzotriazole adducts (2)–(4) and the Grignard reaction products (5)–(7) are collected in Table 2. Overlapping signals have hindered detailed analysis.

The ^{13}C NMR spectrum of the crude adduct (2), shows aliphatic carbon signals at δ 14.1, 20.6, 63.7, and 86.3, with additional lower intensity signals at δ 20.9, 64.4, and 90.9. The latter were assigned to the isomeric compound in which the benzotriazolyl group is bound by its N-2 atom to the α-carbon atom, instead of the N-1 atom, as observed in the main isomer (2). Downfield shifts of the resonances of the (N-2) isomer of 4.55, 0.73, and 0.36 ppm (carbon atoms α, β, and γ, respectively) in relation to the (N-1) isomer reflect the general trend observed in the benzotriazol-1-yl–benzotriazol-2-yl [Bt(1)–Bt(2)] isomerization.[37–39] Integrals of the benzotriazolyl signals[40] of the Bt(1) and Bt(2) isomers in the ^{1}H NMR spectrum, gave the isomer ratio of 10:1, respectively.

Similarly, signals additional to those given in Table 3 were observed in the aliphatic part of the ^{13}C spectrum of crude (3) at δ 24.3, 32.3, 70.2, and 94.2 which were assigned to the tetrahydrofuranyl ring of the benzotriazol-2-yl isomer. The molecular ratio of the Bt(1) to Bt(2) isomers for (3) was 7:1. Additional signals in the aliphatic part of the ^{13}C NMR spectrum of (4) were observed at δ 21.3, 24.6, 29.8, 67.4, and 90.6 with a molar ratio of the Bt(1) to Bt(2) isomers of 3:1. This is in agreement with the previous reports that steric factors play the important role in the Bt(1)–Bt(2) isomerization.[39,41,42]

Comparisons with the literature data allowed full assignment of the ring carbon resonances for the tetrahydro-furan and -pyran derivatives (Table 3). In comparison with unsubstituted tetrahydrofuran,[43] substitution of a C-2 hydrogen by benzotriazol-1-yl (3) shifts the C-2, C-3, C-4, and C-5 resonances by +18.8, +4.6, −1.9, and +0.1 ppm, respectively. Compared with 2-methyltetrahydrofuran,[44] the shifts are smaller: +12.3, −2.7, −1.9, and +1.4 ppm, respectively. The chemical shift differences of the C-2 resonances induced by the methyl and benzotriazol-1-yl groups is caused mainly by the difference in electronegativity between carbon and nitrogen, whereas the strong β-effect[45,46] of the methyl group causes the difference in C-3 resonances.

In comparison with 2-methyltetrahydrofuran,[44] the C-2 signal of (6a) is shifted 3.8 ppm downfield and the C-3 signal 2.2 ppm upfield, reflecting the alkyl group β- and γ-effects.[45,46] The C-4 and C-5 signals of (6a) are almost the same as in 2-methyltetrahydrofuran. Similar regularities were observed in the ^{13}C NMR spectra of the remaining monosubstituted tetrahydrofurans (6b)–(6d). The 'attached proton test' procedure allowed easy distinction of the closely spaced resonances of C-2 and C-5 in the spectra of the 2-alkynyl derivatives (6c) and (6d).

Compared with 2-(methylamino)tetrahydropyran[47] [the closest analogue to (4) with a reported precise analysis of its ^{13}C NMR spectrum], the C-2, C-3, C-4, C-5, and C-6 resonances of (4) are shifted: −4.1, −3.6, −2.3, −1.3, and +0.1 ppm, respectively. These shifts reflect the different electronic properties of the methylamino and benzotriazol-1-yl groups (strongest effect on C-2) and also a difference in the relative stability of the equatorial and axial conformers of 2-(methylamino)tetrahydropyran and (4). The strong influence of molecular conformation on the ^{13}C NMR spectra of 2-substituted tetrahydropyrans, with downfield shifts of C-2, C-3 and C-4 signals of the axial conformers, is well documented.[47]

In comparison with (3), the signals of C-2 and C-3 of 2,5-bis(benzotriazol-1-yl)tetrahydrofuran (13) are very similar. Changing the C-5 benzotriazol-1-yl group for the -2-yl isomer caused a remarkable downfield shift of the C-5 signal, in accordance with our previous observation of the influence of benzotriazolyl isomerization on the ^{13}C NMR spectra of its derivatives.[42,48–50]

In comparison with 2-vinyltetrahydropyran,[51] the C-2 resonance of 2-phenyltetrahydropyran (7a) is shifted downfield (+1.6 ppm). The C-3, C-4, C-5, and C-6 tetrahydropyran ring carbon resonances of alkynyl derivatives [(7b)] and (7c)] occur at fields similar to those reported for 2-ethynyltetrahydropyran,[52] but C-2 are shifted strongly upfield [−5.9 and −6.1

Table 2. ^{1}H NMR spectra[a] of compounds (2)–(7) (Scheme 1).

Compd.	Bt (or R)	Bt–CH–O (or R–CH–O)	CH_2O	Other groups
(2)	7.21 (1 H, t, *J* 7.0) 7.30 (1 H, t, *J* 7.0) 7.64 (1 H, d, *J* 8.0) 7.90 (1 H, d, *J* 8.0)	6.09 (q, *J* 6.1)	3.07 (1 H, q, *J* 7.0) 3.34 (1 H, q, *J* 7.0)	0.94 (3 H, t, *J* 7.0) 1.68 (3 H, d, *J* 6.1)
(3)	7.35 (1 H, dt, *J* 8.2 and 7.0) 7.47 (1 H, dt, *J* 8.2 and 7.0) 7.69 (1 H, dd, *J* 8.2 and 1.1) 8.04 (1 H, dd, *J* 8.2 and 1.1)	6.49 (dd, *J* 8.4 and 1.3)	4.0 (m)	2.17 (1 H, m) 2.45 (2 H, m) 3.12 (1 H, m)
(4)	7.36 (2 H, m) 7.72 (1 H, d, *J* 8.3) 8.05 (1 H, d, *J* 8.3)	6.01 (dd, *J* 8.2 and 2.8)	3.77 (1 H, m) 3.90 (1 H, m)	1.72 (3 H, m) 2.17 (2 H, m) 2.58 (1 H, m)
(5)	0.89 (3 H, t, *J* 6.9) 1.28 (10 H, m)	3.35 (m)	3.43 (1 H, q, *J* 7.0) 3.51 (1 H, q, *J* 7.0)	1.12 (3 H, d, *J* 6.1) 1.19 (3 H, t, *J* 7.0)
(6a)	0.88 (3 H, t, *J* 6.6) 1.29 (10 H, m)	3.78 (m)	3.78 (m)	1.59 (1 H, m) 1.90 (3 H, m)
(6b)	7.30 (5 H, m)	4.86 (t, *J* 7.1)	3.92 (ddd, *J* 14.9, 8.3, and 7.0) 4.06 (ddd, *J* 14.8, 8.1, and 6.7)	1.80 (1 H, m) 1.96 (2 H, quintet, *J* 6.9) 2.30 (1 H, m)
(6c)	7.24 (3 H, m) 7.42 (2 H, m)	4.77 (dd, *J* 7.0 and 5.2)	3.81 (m) 3.95 (m)	2.04 (4 H, m)
(6d)	0.90 (3 H, t, *J* 7.1)	4.55 (m)	3.78 (ddd, *J* 13.2, 7.4, and 5.9)	1.80–2.15 (4 H, m)
(7a)	7.28 (5 H, m)	4.29 (dd, *J* 10.0 and 2.4)	4.12 (1 H, m) 3.58 (1 H, m)	1.59 (4 H, m) 1.82 (1 H, m) 1.91 (1 H, m)
(7b)	7.27 (3 H, m) 7.45 (2 H, m)	4.48 (dd, *J* 7.6 and 3.0)	3.55 (m) 4.02 (m)	1.55 (3 H, m) 1.78 (1 H, m) 1.87 (2 H, m)
(7c)	0.83 (3 H, t, *J* 7.1) 1.45 (4 H, m)	4.22 (m)	3.48 (m) 3.95 (m)	1.50 (4 H, m) 1.82 (2 H, m)

[a] Chemical schifts δ are given in ppm from TMS signal, coupling constants *J* (in brackets) are given in Hz.

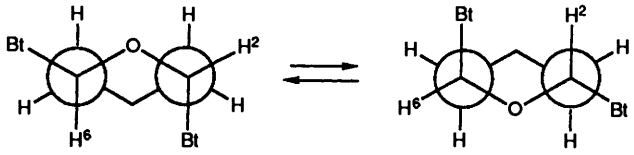
Table 3. ^{13}C NMR spectra[a] of tetrahydrofurans and tetrahydropyrans.

	Cycloether ring atoms					
Compd.	C-2	C-3	C-4	C-5	C-6	Substituents
(3)	87.9	30.8	24.3	69.2	—	110.4, 119.7, 124.1, 127.4, 132.8, 146.3
(4)	85.6	29.2	21.5	24.8	66.7	111.0, 119.7, 124.1, 127.4, 132.3, 146.1
(6a)	79.4	31.3	26.3	67.5	—	14.0, 22.5, 25.6, 29.4, 31.8, 35.7
(6b)	80.5	34.5	25.9	68.5	—	125.5, 126.9, 128.1, 143.3
(6c)	68.5	33.3	25.4	67.8	—	84.4, 89.0, 122.7, 128.1, 131.6, 132.0
(6d)	68.4	33.5	25.3	67.5	—	13.5, 18.2, 21.8, 30.7, 79.8, 85.1
(7a)	80.0	33.9	23.9	25.8	68.8	125.7, 127.1, 128.1, 143.2
(7b)	67.4	32.2	21.8	25.7	66.5	85.2, 88.2, 122.7, 128.2, 131.7, 132.2
(7c)	67.2	32.6	22.0	25.8	66.5	13.6, 18.4, 22.0, 30.8, 79.0, 85.6
(13)	87.5	30.1	30.1	87.5	—	109.5, 119.9, 124.3, 127.9, 132.6, 146.0
(14)[b]	88.2	29.6	31.7	94.6	—	R^1; 109.8, 120.1, 124.4, 128.0, 132.6, 145.9 R^2; 118.5, 127.1, 145.9
(17)[b]	80.1	28.9[c]	17.7	29.3[c]	100.2	Bt; 110.5, 119.7, 124.0, 127.4, 132.1, 146.3 OMe; 55.4
(18)	81.8	27.1	18.9	27.1	81.8	110.2, 119.9, 124.4, 127.7, 132.5, 146.1
(19)[b]	82.2	27.2	18.2	28.3	88.0	Bt(1); 110.7, 119.9, 124.4, 127.9, 132.9, 146.2 Bt(2); 118.5, 127.1, 144.3
(35)	68.2	33.2	33.2	68.2	—	13.5, 18.4, 21.9, 30.6, 79.3, 85.7

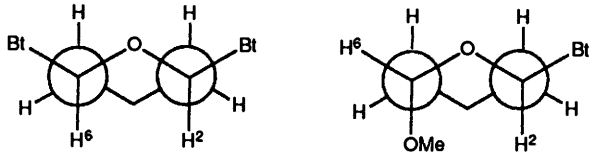
[a] Chemical shifts are given in ppm from the TMS signal. [b] Substituent Bt(1) on C-2. [c] The assignment may be reverse.

ppm, for (7b) and (7c), respectively] indicating the lower electron-withdrawing effect of a substituted alkynyl group.

Disubstituted derivatives of tetrahydrofuran and tetrahydropyran display *cis* and *trans* isomerization. In *cis*- and *trans*-2,5-dimethyltetrahydrofuran,[44] the ^{13}C NMR signals of the two different isomers occur close to each other. In *cis*-2,6-disubstituted tetrahydropyrans, the C-2, C-3, and C-4 signals are reportedly[51,52] almost the same as in 2-monosubstituted derivatives, whereas the *trans* isomer signals are significantly upfield. Comparison of the ^{13}C NMR spectra of adducts (17), (18), and (19) with the spectrum of (4) showed that all these adducts are of the *trans* configuration. Additional support for



(18), two conformers of the *trans* isomer



(18), conformation of the *cis* isomer

(17), predominant *trans* conformation

Figure. Conformations of adducts (**17**) and (**18**) shown in Newman projection.

the structure of bis-adducts (**18**) and (**19**) was obtained from the splitting pattern of the 2-H and 6-H resonances in the ^1H NMR spectra. Similar and relatively small coupling constants of these protons [J 4.0 and 6.3 Hz, for (**18**)] are typical for *gauche* interactions in two equilibrating *trans* conformers (Figure), whereas a large difference of the coupling constants would be expected in the *cis* isomer.[53] In the case of adduct (**17**), the coupling constants of 2-H (J 2.7 and 10.5 Hz) and the small coupling of 6-H (the signal observed as a broadened singlet) can be explained by strong dominance of the conformation with equatorial Bt and axial OMe groups (Figure), caused by severe steric repulsion of the bulky benzotriazol-1-yl substituent in the axial position.

Experimental

M.p.s were determined using a Thomas–Hoover capillary m.p. apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-300 (300 MHz) spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard. The IR spectra were recorded on a Perkin-Elmer 1600 instrument. Low and high resolution mass spectra were determined at 70 eV with an AEI MS-30 mass spectrometer operating with a Kratos DS-55 data system. Elemental analyses were determined by Atlantic Microlab, Norcross, Georgia (liquids) or in the Department of Chemistry (solids) under the supervision of Dr. R. W. King. Solvents (ether, benzene, and toluene) were dried by reflux under nitrogen with sodium–benzophenone and distilled immediately prior to use.

Addition of Benzotriazole to Ethyl Vinyl Ether.—A solution of benzotriazole (11.9 g, 100 mmol) and ethyl vinyl ether (14.4 g, 200 mmol) in carbon tetrachloride was refluxed for 1.5 h to give, after evaporation of the solvent, analytically pure 1-ethoxy-1-benzotriazolylethane (**2**) as an oil (a mixture of benzotriazol-1-yl and -2-yl isomers in a ratio of 10:1), with 100% yield.

Addition of Benzotriazole to 2,3-Dihydrofuran.—A mixture of benzotriazole (11.9 g, 100 mmol), 2,3-dihydrofuran (7.5 g, 100 mmol), and carbon tetrachloride (100 ml) was stirred and refluxed for 5 h. Evaporation of the solvent gave 2-benzotriazolyltetrahydrofuran (**3**) as an oil (18.9 g, 100%) which appeared to be a mixture of benzotriazol-1-yl and -2-yl isomers in a ratio of 7:1.

Addition of Benzotriazole to 3,4-Dihydropyran.—A solution of benzotriazole (11.9 g, 100 mmol) and dihydropyran (84.3 g, 120 mmol) in carbon tetrachloride (100 ml) was stirred and refluxed for 2 h to give, after evaporation of the solvent, analytically pure 2-benzotriazolyltetrahydropyran (**4**) as an oil (100%) (a mixture of benzotriazol-1-yl and -2-yl isomers in a ratio of 3:1). After a few days at room temperature, the oil crystallized to form large prisms of the isomerically pure (**4**) (benzotriazol-1-yl derivative), m.p. 55 °C.

Reaction of 1-Ethoxy-1-benzotriazolylethane (**2**) *with Hexylmagnesium Iodide.*—To a solution of 1-(benzotriazol-1-yl)-1-ethoxyethane (9.6 g, 50 mmol) in benzene (100 ml) was added, portionwise, a Grignard reagent prepared from 1-iodohexane (22.1 ml, 150 mmol) and magnesium turnings (2.48 g, 200 mmol) in dry ether (125 ml). After the addition of the Grignard reagent, more dry benzene (100 ml) was added, and the ethyl ether was distilled off until the distillate temperature reached 75 °C. The reaction mixture was then poured into ice–water (100 ml) and neutralized with acetic acid. The organic layer was separated, washed with water, followed by sodium carbonate (10%; 100 ml) and water again, and dried (Na_2SO_4). Evaporation of the solvent gave a crude product (13.8 g), consisting of 2-ethoxyoctane (**5**) and dodecane in a molar ratio of 1:1. The total yield, according to NMR, was >95%. An analytical sample of (**5**) was prepared by column chromatography (silica gel, methylene dichloride) of the crude mixture. The final yield of (**5**), after chromatography, was 65%.

Reaction of 2-Benzotriazolyltetrahydrofuran (**3**) *with the Hexylmagnesium Iodide.*—To a stirred solution of (**3**) (5.3 g, 25 mmol) in dry ethyl ether (50 ml) in a three-necked round-bottom flask, equipped with a dropping funnel, a heating mantle, a reflux condenser and a mechanical stirrer, was added a Grignard reagent prepared from hexyl iodide (7.4 ml, 50 mmol), magnesium turnings (1.5 g, 60 mmol), and iodine (0.6 g, 2.5 mmol) in dry ether (100 ml) and benzene (100 ml). The mixture was stirred at reflux for 36 h (60 °C) and then poured into ice–water (100 ml). The obtained mixture was neutralized with acetic acid and the organic layer was separated. The obtained solution was washed with water followed by sodium carbonate (10%) and again water, and dried (Na_2SO_4). Evaporation of the solvent gave the crude product (5.1 g); mainly 2-hexyltetrahydrofuran (**6a**) (yield 59%; established by NMR) and dodecane. An analytical sample of (**6a**) was prepared by column chromatography, using silica gel and 2 solvents as eluants: (i) hexanes (to remove dodecane) and (ii) methylene dichloride for 2-hexyltetrahydrofuran.

Reactions of Benzotriazolyl Adducts (**3**) *and* (**4**) *with Iodomagnesium Acetylenides: General Procedure.*—Phenylacetylene (4.4 ml, 40 mmol) (or equivalent amount of hex-1-yne) was added dropwise to a stirred solution of methylmagnesium iodide prepared from methyl iodide (2.5 ml, 40 mmol), magnesium turnings (1.2 g, 50 mmol) and iodine (0.5 g, 2 mmol) in dry ethyl ether (100 ml), and the obtained mixture was stirred for 2 h at 25 °C. Benzotriazole adduct (**3**) or (**4**) (20 mmol) in dry benzene (100 ml) was then added portionwise, and the mixture was stirred at reflux (55–60 °C) for 24 h. The reaction mixture was poured into ice–water (100 ml), neutralized with acetic acid, and ethyl ether (100 ml) was added. The organic layer was separated, washed with water, then with aqueous sodium carbonate (10%) and again with water, and dried (Na_2SO_4) (20 g) to give, after evaporation of the solvent, a crude product which was then purified by column chromatography (silica gel, toluene).

Condensation of 2,5-Dimethoxytetrahydrofuran with Benzotriazole.—A solution of benzotriazole (29.76 g, 250 mmol) and

toluene-*p*-sulphonic acid (0.19 g, 1 mmol) in 2,5-dimethoxyfuran (51.10 g, 500 mmol) was heated under a distillation apparatus equipped with a fractionating column until no more methanol came over (1.5 h). A sample of the mixture (10.00 g) was subjected to column chromatography (silica gel; toluene–ethyl acetate, 6:1) to give as the first fraction 2-(*benzotriazol*-1-*yl*)-5-(*benzotriazol*-2-*yl*)*tetrahydrofuran* (**14**) (0.82 g, 9%), m.p. 108–110 °C (Found: C, 62.8; H, 4.8; N, 27.1. $C_{16}H_{14}N_6O$ requires C, 62.7; H, 4.6; N, 27.4%); δ 2.90 (1 H, m, 3-H), 3.55 (3 H, m, 3-H and 4-H), 6.82 (1 H, dd, *J* 1.5 and 7.0 Hz, 2-H), 6.94 (1 H, dd, *J* 2.2 and 6.7 Hz, 5-H), 7.43 [3 H, m, Bt(2) and Bt(1)], 7.53 [1 H, ddd, *J* 1.0, 6.9, and 8.0 Hz, Bt(1)], 7.69 [1 H, ddd, *J* 1.0, 1.9, and 8.3 Hz, Bt(1)], 7.92 (2 H, m, Bt-2), and 8.11 [1 H, ddd, *J* 1.0, 1.9, and 8.3 Hz, Bt(1)].

The second fraction gave 2,5-*bis*(*benzotriazol*-1-*yl*)*tetrahydrofuran* (**13**) (3.62 g, 36%) which was recrystallized from methanol to give prisms, m.p. 137–142 °C (Found: C, 62.9; H, 4.7; N, 27.8. $C_{16}H_{14}N_6O$ requires C, 62.7; H, 4.6; N, 27.4%); δ 3.33 (4 H, br s, 3-H and 4-H), 6.74 (2 H, br s, 2-H and 5-H), 7.41 (2 H, t, *J* 8.0 Hz, Bt), 7.52 (2 H, t, *J* 6.8, Bt), 7.62 (2 H, d, *J* 8.1, Bt), 8.08 (2 H, dd, *J* 1.0 and 8.3 Hz, Bt).

The third fraction was a colourless oil which upon trituration with ether–pentane (1:1) gave white needles of 1,4-*bis*(*benzotriazol*-1-*yl*)-1,4-*dimethoxybutane* (**16**) (3.00 g, 30%), m.p. 146–148 °C (Found: C, 61.8; H, 5.8; N, 23.8. $C_{18}H_{20}N_6O_2$ requires C, 61.4; H, 5.7; N, 23.8%); δ_H 2.31 (4 H, m, CH_2CH_2), 3.22 (6 H, s, 2 × OCH_3), 5.99 (2 H, br s, 2 × NCHO), 7.40 (2 H, t, *J* 7.1 Hz, Bt), 7.49 (2 H, t, *J* 7.0, Bt), 7.68 (2 H, dd, *J* 1.0 and 8.2 Hz, Bt), and 8.09 (2 H, dd, *J* 1.0 and 8.2 Hz); δ_C 30.3 (CH_2), 56.6 (OCH_3), 91.3 (NCO), 110.9, 120.2, 124.4, 127.8, 131.2, and 146.7.

Addition of Benzotriazole to 2-Methoxy-3,4-dihydropyran.—Benzotriazole (29.8 g, 250 mmol) and 2-methoxy-3,4-dihydropyran (28.5 ml, 250 mmol) in carbon tetrachloride (250 ml) was stirred and refluxed for 3 h. Evaporation of the solvent gave the crude product (60.5 g) as an oil (mixture of isomers, according to NMR). After trituration of the crude product with a mixture of ethyl ether and n-hexane (125 + 25 ml) and cooling in a freezer for 4 h, creamy crystals precipitated. The crystals were filtered off and dried to give 2-(*benzotriazol*-1-*yl*)-6-*methoxytetrahydropyran* (**17**) (23.1 g, 40%), m.p. 69–70 °C (Found: C, 61.5; H, 6.5; N, 18.1. $C_{12}H_{15}N_3O_2$ requires C, 61.8; H, 6.5; N, 18.0%); δ_H 1.89 (3 H, m), 2.16 (2 H, m), 2.57 (1 H, m), 3.50 (3 H, s, OCH_3), 4.91 (1 H, br s, 6-H), 6.41 (1 H, dd, *J* 2.7, and 10.5 Hz, 2-H), 7.37 (1 H, ddd, *J* 1.2, 6.9, and 8.3 Hz, Bt), 7.50 (1 H, ddd, *J* 1.0, 6.9, and 8.0 Hz, Bt), 7.73 (1 H, ddd, *J* 1.1, 1.9, and 8.2 Hz, Bt), and 8.07 (1 H, ddd, *J* 1.0, 2.1, and 8.3 Hz, Bt).

Reaction of (**17**) *with Benzotriazole: Adducts* (**18**) *and* (**19**).—A solution of (**17**) (1.17 g, 5 mmol), benzotriazole (1.19 g, 10 mmol) and toluene-*p*-sulphonic acid (0.10 g, 0.5 mmol) in toluene (5 ml) was heated in a flask equipped with a distillation condenser until the distillation temperature reached 90 °C. The reaction mixture was then poured into ice–water (10 ml) and extracted with methylene dichloride (20 ml). The organic layer was separated, washed with aqueous sodium carbonate (10%), followed by water, and dried (Na_2SO_4). Evaporation of the solvent gave an oily product (1.82 g), which was subjected to column chromatography (silica gel, toluene–ethyl acetate, 6:1). The oil obtained as the first fraction appeared to be 2-(*benzotriazol*-1-*yl*)-6-(*benzotriazol*-2-*yl*)*tetrahydropyran* (**19**) (0.04 g, 2.5%) (Found: M^+, 320.1383. $C_{17}H_{16}N_6O$ requires *m/z*, 320.1386); δ_H 1.80 (1 H, m), 2.42 (3 H, m), 2.76 (1 H, m), 2.95 (1 H, m), 6.33 (1 H, dd, *J* 4.0 and 6.7 Hz, 6-H), 6.55 (1 H, dd, *J* 3.6 and 7.6 2-H), 7.39 (4 H, m), 7.62 (1 H, ddd, *J* 1.2, 2.2, and 8.2 Hz), 7.84 [2 H, m, Bt(2)], and 8.14 [1 H, ddd, *J* 1.1, 2.0, and 8.3 Hz, Bt(1)].

The second fraction gave an oil which appeared to be 2,6-*bis*(*benzotriazol*-1-*yl*)*tetrahydropyran* (**18**). Upon trituration with ether and storage at −5 °C, (**18**) crystallized as white grains (0.20 g, 13%), m.p. 123–124 °C (Found: C, 63.4; H, 5.0; N, 26.2. $C_{17}H_{16}N_6O$ requires C, 63.7; H, 5.0; N, 26.2%); δ_H 2.37 (1 H, m), 2.43 (1 H, dd, *J* 4.0 and 7.7 Hz), 2.51 (2 H, dd, *J* 5.9 and 11.6 Hz), 2.98 (1 H, m), 6.17 (2 H, dd, *J* 4.0 and 6.3 Hz, 2-H and 6-H), 7.37 (6 H, m, Bt), and 8.09 (2 H, m, Bt).

Reaction of Benzotriazole with Vinyl Acetate.—A solution of benzotriazole (11.91 g, 100 mmol) and toluene-*p*-sulphonic acid monohydrate (0.19 g, 1 mmol) in vinyl acetate (23.0 ml, 250 mmol) was heated under reflux for 50 h. The reaction mixture was then stored at −5 °C for 10 days. The obtained precipitate was filtered off, washed with ether, and dried in air to give 1,1-*bis*-(*benzotriazol*-1-*yl*)*ethane* (**23a**) (2.00 g, 15%), as colourless cubes, m.p. 140–142 °C (Found: C, 63.3; H, 4.6; N, 31.4. $C_{14}H_{12}N_6$ requires C, 63.6; H, 4.6; N, 31.8%); δ_H 2.74 (3 H, d, *J* 7.0 Hz, CH_3), 7.34 (2 H, dt, *J* 1.0 and 8.2 Hz, Bt), 7.43 (2 H, dt, *J* 1.0 and 7.0 Hz, Bt), 7.69 (2 H, d, *J* 8.3 Hz, Bt), 7.86 (1 H, q, *J* 7.0 Hz, NCHN), and 8.02 (2 H, d, *J* 8.3 Hz, Bt); δ_C 18.3 (CH_3), 68.0 (NCHN), 110.1, 120.2, 124.7, 128.4, 131.4, and 146.6.

After separation of (**23a**), excess of vinyl acetate and volatile products were evaporated from the filtrate to give an oil (15.65 g). A sample of the oil (1.40 g) was subjected to column chromatography (silica gel; methylene dichloride) to give, as the first fraction, 1-*acetylbenzotriazole* (**21**) (0.18 g, 12%), whose ^1H and ^{13}C NMR spectra were identical with the reported ones.[37]

The second fraction appeared to be an unidentified mixture (0.36 g). The third fraction gave 1,1-bis-benzotriazol-1-yl)ethane (**23a**) (0.30 g, 25%), identifiable above. The total yield of (**23a**) was, therefore, 40%.

Reaction of Benzotriazole with Isopropenyl Acetate.—A solution of benzotriazole (11.93 g, 100 mmol) and isopropenyl acetate (20.02, g, 200 mmol) in carbon tetrachloride (200 ml) was heated at reflux for 5 days. The solvent was evaporated to leave an oily product (16.62 g). The oil was set aside at 25 °C for 14 days to give 2-(*benzotriazol*-1-*yl*)-2-(*benzotriazol*-2-*yl*)*propane* (**24b**) (6.40 g, 43%) as colourless cubes, m.p. 162 °C (Found: C, 64.5; H, 5.0; N, 30.5. $C_{15}H_{14}N_6$ requires C, 64.7; H, 5.1; N, 30.2%); δ_H 2.74 (6 H, s, 2 × CH_3), 6.85 [1 H, d, *J* 8.2 Hz, Bt(1)], 7.20 [1 H, ddd, *J* 1.4, 7.0, and 8.3 Hz, Bt(1)], 7.27 [1 H, ddd, *J* 1.3, 7.0, and 8.3 Hz, Bt(1)], 7.40 [2 H, m, Bt(2)], 7.85 [2 H, m, Bt(2)], and 8.05 [1 H, ddd, *J* 1.2, 1.9, and 8.0 Hz, Bt(1)]; δ_C 28.2 (CH_3), 82.4 (NCN), 110.6 [Bt(1)], 118.6 [Bt(2)], 120.2 [Bt(1)], 124.0 [Bt(1)], 127.3 [Bt(2)], 127.7 [Bt(1)], 131.5 [Bt(1)], 144.2 [Bt(2)], and 146.8 [Bt(1)].

Addition of Benzotriazole to Diketene.—A solution of benzotriazole (11.93 g, 100 mmol) and diketene (25.22 g, 300 mmol) in carbon tetrachloride (50 ml) was heated under reflux for 3 h. After cooling, the solution was kept at −5 °C for 24 h to give 1-(*benzotriazol*-1-*yl*)*butane*-1,3-*dione* (**25**) (9.11 g, 94%) as yellowish needles, m.p. 69–70 °C (Found: C, 58.9; H, 4.4; N, 21.1. $C_{10}H_9N_3O$ requires C, 59.1; H, 4.5; N, 20.7%). In deuteriochloroform solutions, the product exists as two tautomers, (**25**) and (**27**), in a ratio of 45:55.

(**25**): δ_H 2.43 (3 H, s, CH_3), 4.56 (2 H, s, CH_2), 7.52 (1 H, t, *J* 6.6 Hz, Bt), 7.67 (1 H, t, *J* 7.4 Hz, Bt), 8.11 (1 H, d, *J* 8.2 Hz, Bt), and 8.29 (1 H, m, Bt); δ_C 30.6 (CH_3), 51.0 (CH_2), 114.2 (Bt), 120.2 (Bt), 126.5 (Bt), 130.7 (Bt), 130.8 (Bt), 146.3 (Bt), 169.2 (Bt–C=O), and 200.2 (CH_3C=O).

(**27**): δ_H 2.19 (3 H, s, CH_3), 6.64 (1 H, s, C–CH=C), 7.48 (1 H, t, *J* 7.6 Hz, Bt), 7.63 (1 H, t, *J* 7.1 Hz, Bt), 8.11 (1 H, d, *J* 8.2 Hz, Bt), and 8.29 (1 H, m, Bt); δ_C 22.3 (CH_3), 90.2 (C–*C*H=C), 114.5

(Bt), 120.0 (Bt), 125.9 (Bt), 130.1 (Bt), 131.1 (Bt), 146.3, 165.8, and 182.1.

Adduct (**25**) (2.03 g, 10 mmol) was added portionwise to a stirred solution of phenylhydrazine (1.08 g, 10 mmol) in absolute ethanol (10 ml), externally cooled in an ice-bath. Stirring at 0–5 °C was continued for an additional 1 h and the mixture set aside at 25 °C for 16 h. After evaporation of the ethanol under reduced pressure, the residue was subjected to column chromatography (silica gel; benzene–ethyl acetate, 4:1) to give 3-*methyl*-1-*phenylpyrazol*-5-*one* (**26**) (1.05 g, 38%) as the first fraction and benzotriazole (**1**) (0.70 g, 59%) as the second fraction.

Reaction of 2-(*Benzotriazol*-1-*yl*)*tetrahydropyran* (**4**) *with Ethylmagnesium Bromide*.—To a stirred solution of ethylmagnesium bromide, prepared from ethyl bromide (43.6 g, 400 mmol), magnesium turnings (12.2 g, 500 mmol), and iodine (8 mmol, 2.1 g) in dry ether (250 ml), was added an ethereal solution of (**4**) (17.0 g, 80 mmol). The reaction mixture was stirred at 25 °C for 24 h. Progress of the reaction was monitored by NMR and TLC. The reaction mixture was poured into ice–water, neutralized with acetic acid, and the ethereal layer was separated. The solution was washed with water, aqueous sodium carbonate (10%), and water again, and dried (Na_2SO_4). Evaporation of the solvent afforded a crude product (12.0 g). A sample of the product (3.4 g) was subjected to column chromatography (silica gel; chloroform) to give (**4**) (0.75 g) as the first fraction. The second fraction, a reddish oil, appeared to be *N*-ethyl-*N*′-(1-hydroxyheptan-5-yl)benzene-1,2-diamine (**33**) (0.90 g, 20%). δ_H 0.93 (3 H, t, *J* 7.3 Hz), 1.28 (3 H, t, *J* 7.1 Hz), 1.53 (8 H, m), 2.80 (2 H, br s, NH), 3.10 (2 H, q, *J* 7.1 Hz), 3.24 (1 H, m), 3.56 (2 H, t, *J* 6.3 Hz), and 6.75 (4 H, m); δ_C 10.0, 15.0, 22.0, 26.8, 32.7, 33.6, 39.0, 53.8, 62.5, 112.0, 112.2, 118.3, 119.1, 136.7, and 137.2.

Another sample of the crude reaction mixture (4.3 g) was stirred and refluxed with carbon disulphide (10 ml) for 24 h. Progress of the reaction was monitored by NMR. After evaporation of the solvent, the crude reaction mixture was separated and purified by column chromatography (silica gel; methylene dichloride) to give the starting material (**4**) (0.85 g) as the first fraction. The second fraction was found to be 3-*ethyl*-1-(1-*hydroxyheptan*-5-*yl*)*benzimidazole*-2-*thione* (**34**) (1.20 g, 18%), a yellowish oil (Found: C, 65.5; H, 8.3; N, 9.5. $C_{16}H_{22}N_2SO$ requires C, 65.7; H, 8.3; N, 9.6%); δ_H 0.81 (3 H, t, *J* 7.3 Hz, CH_3), 1.19 (2 H, m), 1.37 (3 H, t, *J* 7.1 Hz, Et), 1.55 (2 H, m), 1.93 (2 H, m), 2.09 (2 H, m), 3.23 (1 H, br s, OH), 3.49 (2 H, t, *J* 6.3 Hz, C*H*$_2$OH), 4.41 (2 H, q, *J* 7.1 Hz, Et), 5.47 (1 H, m, NCH), 7.23 (3 H, m), and 7.41 (1 H, d, *J* 8.0); δ_C 10.2 (CH_3), 12.2 (CH_3), 21.9, 25.5, 31.6, 32.0, 39.3, 58.3 (NCH), 61.3 (CH_2), 108.5, 110.0, 121.7, 129.6, 131.3, and 169.0 (C=S).

Reaction of Adducts (**13**) *and* (**14**) *with Hexynylmagnesium Iodide*.—A solution of hex-1-ynylmagnesium iodide in ether (150 ml), prepared from magnesium turnings (7.20 g, 300 mmol), methyl iodide (15.7 ml, 250 mmol) and hex-1-yne (28.1 ml, 250 mmol) according to the general procedure given above, was added dropwise to a stirred solution of a crude reaction mixture (**13**), (**14**), and (**16**) (30.60 g) in dry toluene (150 ml). The ether was then distilled off from the reaction mixture, and the remaining toluene solution was heated at reflux under nitrogen for 24 h. The reaction mixture was poured into ice–water (200 g), neutralized with acetic acid, and the organic layer was separated. The obtained toluene solution was washed with water, aqueous sodium carbonate (10%) and dried ($MgSO_4$). Evaporation of the solvent afforded an oily product (18.60 g). A sample of this oil (10.21 g) was subjected to column chromatography (silica gel; toluene–ethyl acetate, 6:1) to give 2,5-*bis*(*hex*-1-*ynyl*)*tetrahydrofuran* (**35**) (0.41 g) as an oil (Found: C, 82.8; H, 10.4. $C_{16}H_{24}O$ requires C, 82.7; H, 10.4%); δ_H 0.89 (6 H, t, *J* 7.1 Hz, 2 × CH_3), 1.45 (8 H, m, 4 × CH_2), 1.92 (2 H, m, 3-H and 4-H), 2.19 (4 H, t, *J* 6.9 Hz, 2 × $CH_2C{\equiv}C$), 2.25 (2 H, m, 3-H and 4-H), and 4.73 (2 H, m, 2-H and 5-H); δ_C 13.5 (CH_3), 18.4, 21.9, 30.6, 33.2, 68.2 (CH–O), 79.3 (C≡C), and 85.7 (C≡C).

The second fraction eluted with the same solvent mixture appeared to be 7,10-dimethoxyhexadeca-5,11-diyne (**36**) (4.58 g), an oil (Found: $M^+ - OCH_3$, 247.2064. $C_{17}H_{27}O$ requires *m*/*z*, 247.2061); δ_H 0.91 (6 H, t, *J* 7.3 Hz, 2 × CH_3), 1.47 (8 H, m, 4 × CH_2), 1.81 (2 H, m), 2.22 (4 H, dt, *J* 1.7 and 6.6 Hz, $CH_2C{\equiv}C$), 3.37 (6 H, s, 2 × CH_3O), and 3.95 (2 H, m, CHO); δ_C 13.5 (CH_3), 18.3, 21.8, 30.7, 31.5, 56.0 (OCH_3), 71.0 (CH–O), 78.5 (C≡C), and 86.9 (C≡C).

Reaction of 2-(*Benzotriazol*-1-*yl*)-6-*methoxytetrahydrofuran* (**17**) *with Phenylmagnesium Bromide*.—A Grignard reagent prepared from magnesium turnings (1.44 g, 60 mmol) and bromobenzene (5.3 ml, 50 mmol) in ether (100 ml) was added dropwise to a stirred solution of (**17**) (5.43 g, 25 mmol) in benzene (100 ml). The reaction mixture was heated under reflux for 45 h but TLC failed to show the occurrence of any reaction. An additional portion of benzene (100 ml) was added to the reaction mixture and the ether was distilled off. The remaining solution was heated under reflux for 24 h and then poured into ice–water. The mixture was neutralized with acetic acid, the organic layer was separated, washed with water, followed by aqueous sodium carbonate (10%) and again water, and dried (Na_2SO_4). Evaporation of the solvent gave an oil which, upon column chromatography (silica gel, methylene dichloride) afforded 5-*methoxy*-1,5-*diphenylpentan*-1-*one* (**37**) (3.52 g, 53%) as an oily fraction (Found: $M^+ - CH_3$, 253.1229. $C_{17}H_{17}O_2$ requires *m*/*z*, 253.1228); δ_H 1.74 (2 H, m), 1.86 (2 H, m), 2.96 (2 H, m, $CH_2C{=}O$), 3.20 (3 H, s, CH_3O), 4.14 (1 H, dd, *J* 5.5 and 7.3 Hz, PhCHO), 7.20–7.60 (8 H, m), and 7.92 (2 H, dd, *J* 1.3 and 7.0 Hz, *o*–PhC=O); δ_C 20.7, 37.6, 38.3, 56.6 (CH_3), 83.9 (PhCHO), 126.6, 127.5, 128.0, 128.4, 128.5, 132.9, 136.9, 142.0, and 200.1 (C=O); *m*/*z* 253 ($M^+ - CH_3$), 237 ($M^+ - OCH_3$), 147, 133, 121 (100%), and 105 (PhC=O).

Reaction of (**17**) *with Phenylethynylmagnesium Iodide*.—To phenylethynylmagnesium iodide obtained from magnesium turnings (3.04 g, 125 mmol), methyl iodide (6.2 ml, 100 mmol), and phenylacetylene (11.0 ml, 100 mmol) in ether (50 ml) according to the general procedure given above, was added a solution of adduct (**17**) (4.67 g, 20 mmol) in toluene (100 ml). The ether was distilled off and the remaining solution was heated at reflux (110 °C) for 3 h. Work-up of the reaction mixture (according to the general procedure) afforded an oil which when subjected to column chromatography (silica gel, toluene–chloroform, 8:1) gave 7-methoxy-1,9-diphenylnona-1,8-diyn-3-ol (**38**) (3.02 g, 47%), as a yellowish oil (Found: M^+, 318.1606. $C_{22}H_{22}O_2$ requires *m*/*z*, 318.1620); δ_H 1.80 (2 H, m), 1.87 (4 H, m), 2.82 (1 H, br s, OH), 3.46 (3 H, s, OMe), 4.19 (1 H, t, *J* 6.2 Hz, C*H*OMe), 4.62 (1 H, t, *J* 5.9 Hz, C*H*OH), 7.25 (6 H, m, Ph); δ_C 21.1, 35.0, 37.3, 56.3 (OMe), 62.5 (COH), 71.5 (*C*Me), 84.7, 86.0, 87.6, 90.1, 122.5 (2 × Ph-*ipso*), 128.11 (2 × Ph-*meta*), 128.14 (2 × Ph-*para*), 131.5 (Ph-*ortho*) and 131.6 (Ph-*ortho*); ν_{max} 3 396 (OH), 3 057 (Ph), 2 935, 2 864, 2 822, 2 227 (C≡C), 1 490, 1 442, 1 339, 1 107, 1 026, 756 (Ph), and 691 (Ph); *m*/*z* 318 (12, M^+), 300 (12, $M^+ - H_2O$), 286 (60, M^+ – MeOH), 269 (49, $M^+ - H_2O$ – MeO), 257 (34), 247 (16), 229 (22), and 145 (100, PhC≡CCH=O$^+$–Me).

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